10663605

=> d his

(FILE 'HOME' ENTERED AT 13:40:37 ON 02 JUN 2004)

FILE 'REGISTRY' ENTERED AT 13:40:55 ON 02 JUN 2004
L1 STRUCTURE UPLOADED
L2 4 S L1
L3 74 S L1 SSS FULL
L4 STRUCTURE UPLOADED
L5 0 S L4 SUB=L3 SAMPLE
L6 6 S L4 SSS FULL SUB=L3
L7 STRUCTURE UPLOADED
L8 0 S L7 SUB=L3 SAMPLE
L9 6 S L7 SSS FULL SUB=L3

FILE 'CAPLUS' ENTERED AT 13:48:34 ON 02 JUN 2004
L10 8 S L6
L11 15 S L9
L12 18 S L10 OR L11

FILE 'REGISTRY' ENTERED AT 14:35:14 ON 02 JUN 2004
L13 STRUCTURE UPLOADED
L14 1 S L13
L15 19 S L13 SSS FULL

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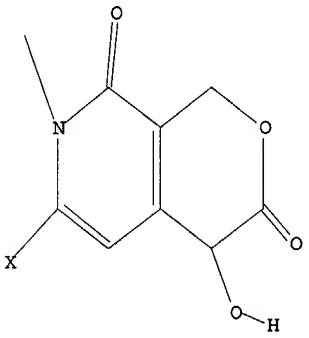
L13 HAS NO ANSWERS
L13 STR



10663605

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=> d his

     (FILE 'HOME' ENTERED AT 13:40:37 ON 02 JUN 2004)

     FILE 'REGISTRY' ENTERED AT 13:40:55 ON 02 JUN 2004
L1               STRUCTURE UPLOADED
L2             4 S L1
L3            74 S L1 SSS FULL
L4               STRUCTURE UPLOADED
L5             0 S L4  SUB=L3 SAMPLE
L6             6 S L4 SSS FULL SUB=L3
L7               STRUCTURE UPLOADED
L8             0 S L7  SUB=L3 SAMPLE
L9             6 S L7 SSS FULL SUB=L3

     FILE 'CAPLUS' ENTERED AT 13:48:34 ON 02 JUN 2004
L10            8 S L6

=> s l9
L11           15 L9

=> s l10 or l11
L12           18 L10 OR L11

=> d l1
L1 HAS NO ANSWERS
L1               STR
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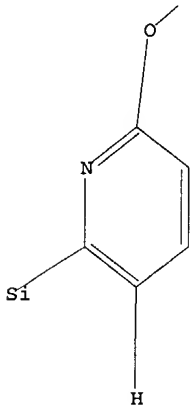

Structure attributes must be viewed using STN Express query preparation.

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L4               STR
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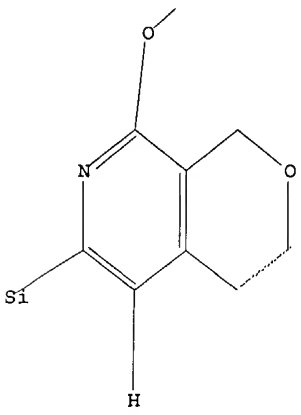

G1 Cl,Br,F,I

10663605

Structure attributes must be viewed using STN Express query preparation.

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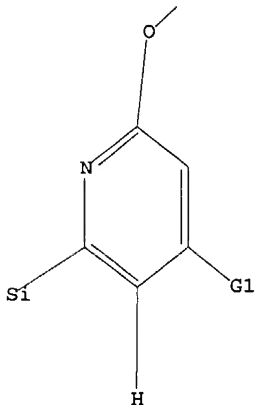
L7 HAS NO ANSWERS
L7 STR



Gl Cl,Br,F,I

Structure attributes must be viewed using STN Express query preparation.

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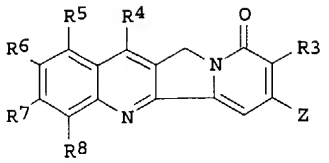
L12 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:719482 CAPLUS
DN 139:246140
TI Preparation of mappicine analogs and intermediates thereof for their therapeutic use as antiviral agents
IN Curran, Dennis P.; Parniak, Michael A.; Gabarda, Ana; Zhang, Wei; Luo, Zhiyong; Hiu-tung, Chen Christine
PA University of Pittsburgh, USA; Fluorous Techonologies Inc.
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003074524	A2	20030912	WO 2003-US6442	20030303
	WO 2003074524	A3	20040429		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004077674	A1	20040422	US 2003-378221	20030303
PRAI	US 2002-360942P	P	20020301		

OS MARPAT 139:246140
GI



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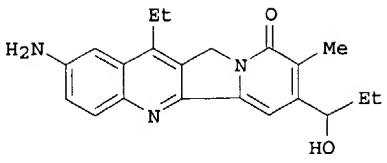


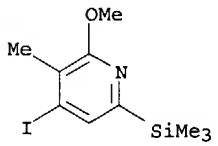
II

AB The present invention discloses preparation of mappicine analogs, such as I [Z = CHOR1R2, C(O)R2; R1 = alkyl, aryl, OC(O)ORa; Ra = alkyl, C(O)Rb; Rb = alkyl, aryl, alkoxy, amino, alkylamino; arylamino, arylalkylamino, protecting group, a fluorous tag; R2 = alkyl, aryl, arylalkyl; R3 = H, alkyl, hydroxyalkyl, aryl; R4-R8 = H, alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, acyloxy, haloalkyl, perfluoroalkyl, halo, haloalkyloxy, carbamoyloxy, OH, NO2, CN, cyanoalkyl, azido, azidoalkyl, formyl, hydrazino, hydrazinoalkyl, hydroxyalkyl, alkoxyalkyl, alkylamino, arylamino, OC(O)OR9; R9 = alkyl, C(O)Rb, SRC, S(O)Rc, S(O2)Rc; Rc = H, C(O)Rb, alkyl, aryl, (CH2)nSiRdReRf; n = 0-10; Rd, Re, Rf = alkyl, alkenyl, alkynyl, aryl, haloalkyl, cyanoalkyl, azidoalkyl, hydrazinoalkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl; R4R5, R6R6, R6R7, R7R8 = a chain of 3 or 4 groups selected from CH, CH2, O, S, N, NH, N-alkyl, N-aryl], and intermediates thereof. Thus, mappicine analog II was prepared and tested for antiviral activity. II showed, in vitro, an IC50 = 10 μM against HIV RNase H, and EC50 = 5 μM against HIV-1 replication.

IT **305816-04-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of mappicine analogs and intermediates thereof for their therapeutic use as RNase H inhibitors)

RN 305816-04-0 CAPLUS

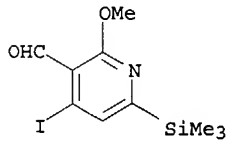
CN Pyridine, 4-iodo-2-methoxy-3-methyl-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of mappicine analogs and intermediates thereof for their therapeutic use as RNase H inhibitors)

RN 174092-75-2 CAPLUS

CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

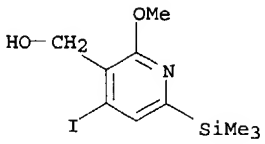


IT **375346-05-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of mappicine analogs and intermediates thereof for their therapeutic use as RNase H inhibitors)

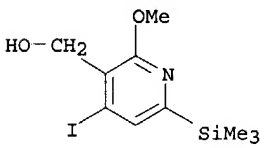
RN 375346-05-7 CAPLUS

CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

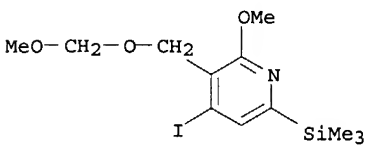
10663605



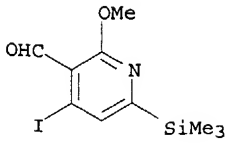
L12 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:482100 CAPLUS
DN 139:180223
TI Solution-Phase Parallel Synthesis of 115 Homosilatecan Analogues
AU Gabarda, Ana E.; Curran, Dennis P.
CS Department of Chemistry and Center of Combinatorial Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Journal of Combinatorial Chemistry (2003), 5(5), 617-624
CODEN: JCCHFF; ISSN: 1520-4766
PB American Chemical Society
DT Journal
LA English
OS CASREACT 139:180223
AB The parallel synthesis of 115 homosilatecans on 1-5 mg scale was accomplished. Key reactions include N-propargylation of a common iodopyridone lactone with a silyl-substituted propargyl bromide, followed by cascade radical annulation with a substituted isonitrile. Simple manual techniques for parallel reactions were coupled with automated purifications (SPE, HPLC) to give high-purity final products. The speed and simplicity of the automated purification protocol more than compensated for yield losses in the synthesis of some analogs relative to traditional flash chromatog. purifications.
IT **375346-05-7P 412046-40-3P**
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of a combinatorial library of homosilatecans from iodopyridone lactones via N-propargylation and cascade radical cyclization)
RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 412046-40-3 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-[(methoxymethoxy)methyl]-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



IT **174092-75-2**
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(preparation of a combinatorial library of homosilatecans from iodopyridone lactones via N-propargylation and cascade radical cyclization)
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:173586 CAPLUS
DN 138:221736
TI Enantioselective synthesis of intermediates of (20R)-homocamptothecins and (20R)-homocamptothecins
IN Curran, Dennis P.; Gabarda, Ana E.
PA University of Pittsburgh, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003018559	A2	20030306	WO 2002-US26424	20020819
	WO 2003018559	A3	20040311		
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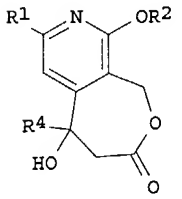
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003073840	A1	20030417	US 2001-940059	20010827
	US 6723853	B2	20040420		
PRAI	US 2001-940059	A	20010827		

OS CASREACT 138:221736; MARPAT 138:221736
GI



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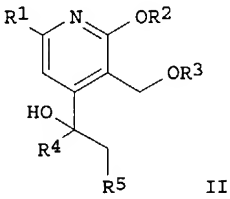
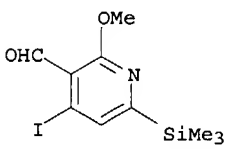


II

AB Intermediates of (20R)-homocamptothecins of formula I [R1 = H, F, Cl, trialkylsilyl; R2, R4 = alkyl] are prepared from compds. of formula II [R3 = protecting group; R5 = carboxylic acid alkyl or aryl ester] by treatment with an organic acid or an inorg. acid.

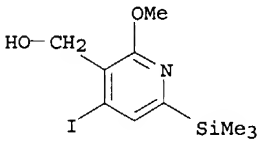
IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(enantioselective synthesis of intermediates of (20R)-homocamptothecins)

RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

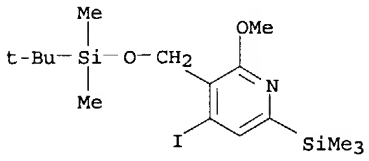


IT **375346-05-7P 375346-06-8P 412046-40-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective synthesis of intermediates of (20R)-homocamptothecins)

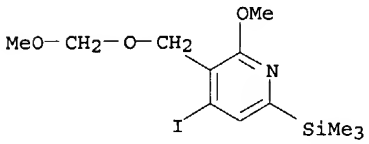
RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



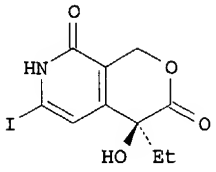
RN 375346-06-8 CAPLUS
CN Pyridine, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 412046-40-3 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-[(methoxymethoxy)methyl]-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



L12 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:27181 CAPLUS
DN 138:338325
TI Catalytic enantioselective synthesis of (20S)-camptothecin intermediates using cyanosilylation of ketones promoted by D-glucose-derived lanthanide catalyst
AU Yabu, Kazuo; Masumoto, Shuji; Kanai, Motomu; Du, Wu; Curran, Dennis P.; Shibasaki, Masakatsu
CS Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, 113-0033, Japan
SO Heterocycles (2003), 59(1), 369-385
CODEN: HTCYAM; ISSN: 0385-5414
PB Japan Institute of Heterocyclic Chemistry
DT Journal
LA English
OS CASREACT 138:338325
GI



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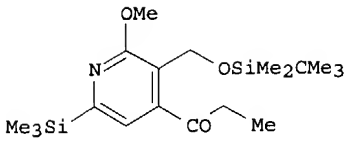

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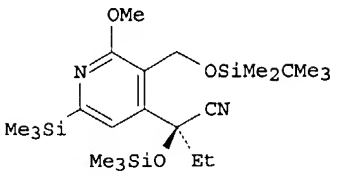
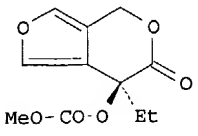


III



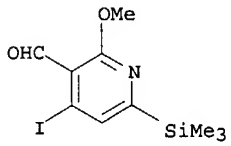
IV

AB An efficient catalytic enantioselective synthetic route was developed for Curran's versatile camptothecin intermediate I. The key step is the catalytic enantioselective cyanosilylation of ketone II using a chiral samarium (Sm) complex. The target ketone cyanohydrin III was obtained with 90% ee using 2 mol% of the catalyst. A gadolinium (Gd) complex derived from the same chiral ligand could also be used as an enantioselective catalyst to synthesize Corey's intermediate IV.

IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. synthesis of (20S)-camptothecin intermediates via cyanosilylation of ketones promoted by in situ formed complexes of lanthanide isopropoxides with D-glucose derived ligands as catalysts)

RN 174092-75-2 CAPLUS

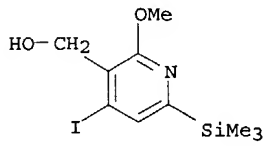
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



IT **375346-05-7P 375346-06-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of (20S)-camptothecin intermediates via cyanosilylation of ketones promoted by in situ formed complexes of lanthanide isopropoxides with D-glucose derived ligands as catalysts)

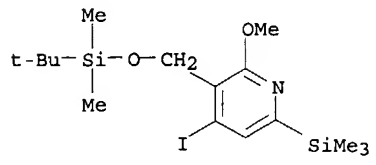
RN 375346-05-7 CAPLUS

CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 375346-06-8 CAPLUS

CN Pyridine, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:658068 CAPLUS
DN 137:201293
TI Method of synthesizing camptothecin-relating compounds
IN Ogawa, Takanori; Nishiyama, Hiroyuki; Uchida, Miyuki; Sawada, Seigo
PA Kabushiki Kaisha Yakult Honsha, Japan
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002066416	A1	20020829	WO 2002-JP1538	20020221
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EE 200300373	A	20031015	EE 2003-373	20020221
	EP 1378505	A1	20040107	EP 2002-703874	20020221
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	NO 2003003579	A	20031010	NO 2003-3579	20030813
PRAI	JP 2001-45430	A	20010221		
	JP 2001-309322	A	20011005		
	WO 2002-JP1538	W	20020221		

OS CASREACT 137:201293; MARPAT 137:201293
GI

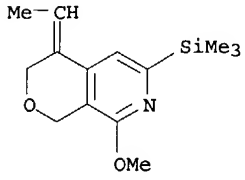
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB 2'-Amino-5'-hydroxypropiophenone (I) corresponding to the AB cycle moiety of the camptothecin (CPT) skeleton and a tricyclic ketone, namely (S)-4-ethyl-7,8-dihydro-4-hydroxy-1H-pyrano[3,4-f]indolizine-3,6,10(4H)-trione (II) corresponding to the CDE cycle moiety thereof can be efficiently produced and thus CPT and its derivs. can be stably supplied by a practically usable total synthesis to more efficiently provide camptothecin (CPT), which is a starting compound for irinotecan hydrochloride, namely 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyloxycamptothecin hydrochloride trihydrate, and various camptothecin derivs. Thus, benzylation of 2-nitro-5-hydroxybenzaldehyde by benzyl chloride in the presence of K2CO3 in DMF at 60° for 20 h gave 94% 5-benzyloxy-2-nitrobenzaldehyde which went addition reaction with vinylmagnesium bromide in THF at 3-10° for 1 h to give 84.0% 1-(5-benzyloxy-2-nitrophenyl)-2-propen-1-ol (VIII). Oxidation of VIII with MnO2 in CHCl3 at 25° for 15 h gave 91% 1-(5-benzyloxy-2-nitrophenyl)-1-oxo-2-propene which was hydrogenated over 10% Pd-C in EtOAc under H atmospheric for 13 h to give 81% I. K2OsO4.2H2O and (DHQD)2PYR were added to an aqueous solution of K3Fe(CN)6, K2CO3, and MeSO2NH2 and stirred at .apprx.5° for 1 h, followed by adding 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, and the resulting mixture was stirred at 5° for 20 h, treated with sodium sulfite, and stirred at 5° for 30 min for asym. dihydroxylation to give a diol (III) (95%) which was oxidized by iodine and K2CO3 in aqueous methanol at 40° for 48 h to give a lactone (IV; R = TMS) (88%). Iodination of IV (R = TMS) by iodine and CF3CO2Ag in CH2Cl2 at room temperature for 16.5 h gave IV (R = iodo) (97%) which underwent carbonylation by CO in the presence of Pd(OAc)2 and K2CO3 in 1-propanol at 60° for 18 to give an ester IV (R = n-PrO2C) (70%). Demethylation of IV (R = n-PrO2C) by treatment with Me3SiCl and NaI in MeCN at room temperature for 3 h gave a keto lactone, namely 4-ethyl-3,4,7,8-tetrahydro-4-hydroxy-3,8-dioxo-1H-pyrano[3,4-c]pyridine-6-carboxylic acid Pr ester (V) (95%) which was cyclocondensed with tert-Bu acrylate in the presence of K2CO3 in DMSO at 50° for 20 min to give a tricyclic compound (VI) (77%). VI was heated with a mixture of CF3CO2H and PhMe at 110° for 100 min to give 77% II which was cyclocondensed

with I in a 1:1 mixture of AcOH and toluene in the presence of p-toluenesulfonic acid monohydrate at 100° for 18 h to give SN-38 (VII; R1= H). VII (R1= H) was converted into irinotecan hydrochloride, VII.HCl (R1 = Q).

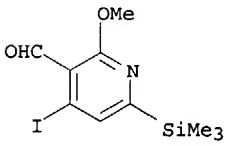
IT **453518-23-5P**
RL: BYP (Byproduct); PREP (Preparation)
(preparation of camptothecin-relating compds. such as irinotecan hydrochloride and intermediates thereof)

RN 453518-23-5 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethylidene-3,4-dihydro-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

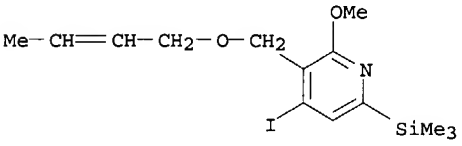


IT **174092-75-2P**, 4-Iodo-2-methoxy-6-trimethylsilyl-3-pyridinecarboxaldehyde **174092-76-3P 174092-77-4P 174092-78-5P 375346-05-7P 453518-24-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of camptothecin-relating compds. such as irinotecan hydrochloride and intermediates thereof)

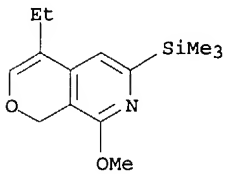
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 174092-76-3 CAPLUS
CN Pyridine, 3-[(2-butenyloxy)methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



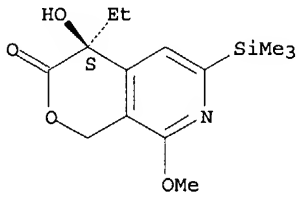
RN 174092-77-4 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



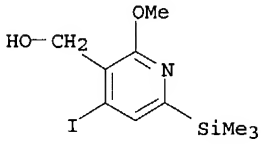
RN 174092-78-5 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (4S)- (9CI) (CA INDEX NAME)

10663605

Absolute stereochemistry. Rotation (+).

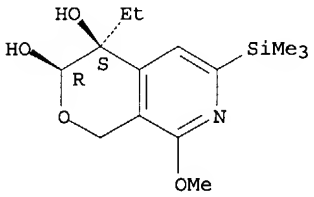


RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



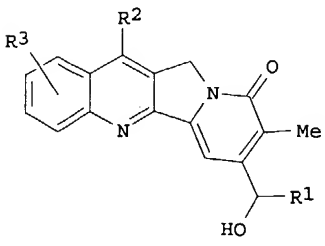
RN 453518-24-6 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine-3,4-diol, 4-ethyl-3,4-dihydro-8-methoxy-6-(trimethylsilyl)-, (3R,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:587848 CAPLUS
DN 137:263220
TI Solution-Phase Preparation of a 560-Compound Library of Individual Pure Mappicine Analogues by Fluorous Mixture Synthesis
AU Zhang, Wei; Luo, Zhiyong; Chen, Christine Hiu-Tung; Curran, Dennis P.
CS Fluorous Technologies Inc., Pittsburgh, PA, 15238, USA
SO Journal of the American Chemical Society (2002), 124(35), 10443-10450
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
GI

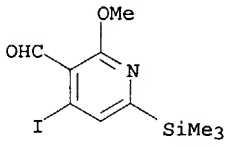


I

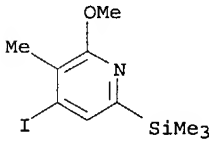
AB Solution-phase mixture synthesis has efficiency advantages and favorable reaction kinetics. Applications of this technique, however, have been discouraged by the difficulty in obtaining individual, pure final products by using conventional separation and identification processes. Introduced here is a new strategy for mixture synthesis that addresses the separation and identification problems. Members of a series of organic substrates are paired with a series of fluorous tags of different chain lengths. The tagged starting materials are then mixed and taken through a multistep reaction process. Fluorous chromatog. is used to demix the tagged product mixts. on the basis of the fluorine content of the tags to provide the individual pure components of the mixture, which are detagged to release the final products. The utility of fluorous mixture synthesis is demonstrated by the preparation of a 560-membered library of analogs of the natural product mappicine, I (R1 = Me, cyclohexyl, Et, etc., R2 = H, Ph, 3-MeOC6H4, etc., R3 = H, 4-Et, 2-F, etc., Rf = C3F7, C6F13, C10F21, etc.). A seven-component mixture is carried through a four-step mixture synthesis (two one-pot and two parallel steps) to incorporate two addnl. points of diversity onto the tetracyclic core. Methods for anal. and purification of the intermediates are established for the quality control of the mixture synthesis.

IT **174092-75-2P 305816-04-0P 375346-05-7P**
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(solution-phase preparation of mappicine analog library using fluorous mixture synthesis)

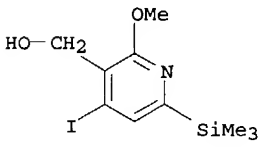
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 305816-04-0 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-methyl-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:585460 CAPLUS
DN 137:311068
TI Asymmetric total synthesis of (20R)-homocamptothecin, substituted homocamptothecins and homosilatecans
AU Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran,

10663605

Dennis P.

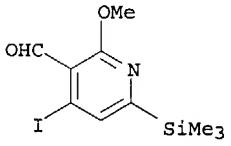
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SO Tetrahedron (2002), 58(32), 6329-6341
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English

AB An efficient asym. synthesis of a key DE lactone pyridone intermediate in the synthesis of homocamptothecin is reported. The synthesis is scalable and features a Stille coupling and a Sharpless asym. epoxidn. as the key steps. The key intermediate was parlayed into homocamptothecin and an assortment of fluorinated homocamptothecins and homosilatecans (7-silylhomocamptothecins), thereby providing the first asym. entry to this important new class of antitumor agents.

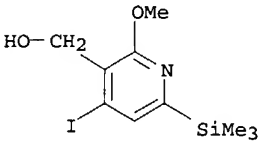
IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(asym. total synthesis of (20R)-homocamptothecin and analogs through a key DE lactone pyridone intermediate using a Stille coupling and a Sharpless asym. epoxidn.)

RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

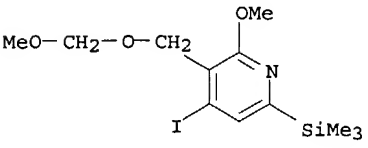


IT **375346-05-7P 412046-40-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. total synthesis of (20R)-homocamptothecin and analogs through a key DE lactone pyridone intermediate using a Stille coupling and a Sharpless asym. epoxidn.)

RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 412046-40-3 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-[(methoxymethoxy)methyl]-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

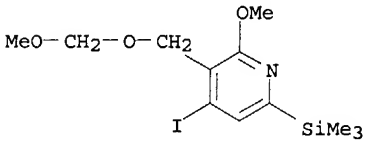


RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:883547 CAPLUS
DN 136:318813
TI Synthesis and evaluation of a novel E-ring modified α-hydroxy keto ether analogue of camptothecin
AU Du, Wu; Curran, Dennis P.; Bevins, Robert L.; Zimmer, Stephen G.; Zhang, Junhong; Burke, Thomas G.

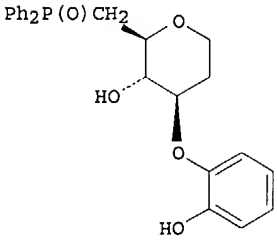
10663605

CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Bioorganic & Medicinal Chemistry (2001), Volume Date 2002, 10(1), 103-110
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB The synthesis of a novel E-ring modified keto ether analog of camptothecin and homocamptothecin by the cascade radical annulation route is reported. The analog, Du 1441, is an isomer of homocamptothecin, but includes the α-hydroxy carbonyl functionality that camptothecin possesses and homocamptothecin lacks. Despite these similarities, the new keto ether analog is inactive in cell assays, and implications for the structure/activity relation are discussed.
IT **412046-40-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and evaluation of a novel E-ring modified α-hydroxy keto ether analog of camptothecin as antitumor agents)
RN 412046-40-3 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-[(methoxymethoxy)methyl]-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

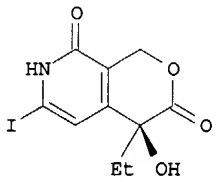


RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:672551 CAPLUS
DN 136:6191
TI Switching Enantiofacial Selectivities Using One Chiral Source: Catalytic Enantioselective Synthesis of the Key Intermediate for (20S)-Camptothecin Family by (S)-Selective Cyanosilylation of Ketones
AU Yabu, Kazuo; Masumoto, Shuji; Yamasaki, Shingo; Hamashima, Yoshitaka; Kanai, Motomu; Du, Wu; Curran, Dennis P.; Shibasaki, Masakatsu
CS Graduate School of Pharmaceutical Sciences, The University of Tokyo, Hongo Bankyo-ku Tokyo, 113-0033, Japan
SO Journal of the American Chemical Society (2001), 123(40), 9908-9909
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:6191
GI



I

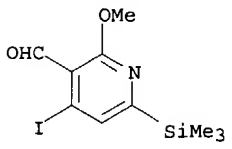


II

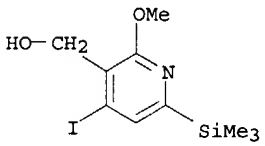
AB A (S)-selective cyanocyclization of ketones was developed utilizing a Gd(O-iPr)3-I complex. The method was used for enantioselective synthesis of the intermediate II for the camtpothecin family.
IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(enantioselective synthesis of key intermediate for (20S)-camptothecin family by (S)-selective cyanosilylation of ketones)
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA

10663605

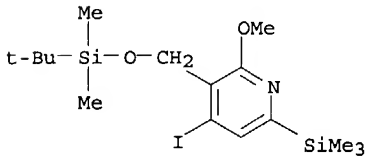
INDEX NAME)



IT **375346-05-7P 375346-06-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(enantioselective synthesis of key intermediate for (20S)-camptothecin family by (S)-selective cyanosilylation of ketones)
RN 375346-05-7 CAPLUS
CN 3-Pyridinemethanol, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 375346-06-8 CAPLUS
CN Pyridine, 3-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:618274 CAPLUS
DN 135:195695
TI Fluorous reaction and separation methods
IN Curran, Dennis P.; De Frutos Garcia, Oscar; Oderaotoshi, Yoji
PA University of Pittsburgh, USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001061332	A1	20010823	WO 2001-US5065	20010216
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1269170	A1	20030102	EP 2001-910849	20010216
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	JP 2003523350	T2	20030805	JP 2001-560670	20010216
PRAI	US 2000-506779	A	20000218		
	WO 2001-US5065	W	20010216		

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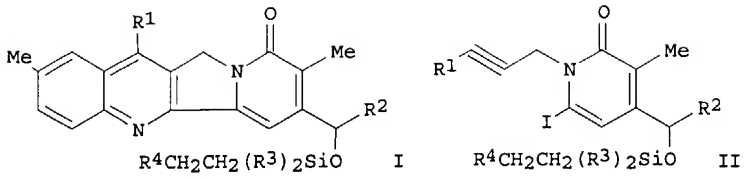
GI

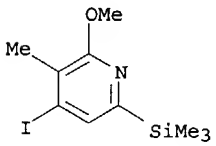


AB The present invention provides a fluorous-tagging strategy comprising the steps of: a. tagging a first organic compound with a first tagging moiety to result in a first tagged compound; b. tagging at least a second organic compound with a second tagging moiety different from the first tagging moiety to result in a second tagged compound; and c. separating the first tagged compound from a mixture including the second tagged compound using a separation technique based upon differences between the first tagging moiety and the second tagging moiety, in the synthesis and separation of mixts. of organic compds. including analogs of mappicine, such as, [I; R1 = H, aryl, SiMe2Bu-t; R2 = alkyl, CH2Ph; R3 = alkyl; R4 = alkyl, fluoroalkyl]. Thus, mappicine analogs, such as, I [R1 = H, Ph, SiMe2Bu-t; R2 = Et, Bu-t, CH2Ph; R3 = Me, (Me)2CH,; R4 = C6H13, C4F9, C6F13, C8F17, C10F21] were prepared via radical cyclization of N-alkylated pyridone [II; R1 = H, Ph, SiMe2Bu-t; R2 = Et, Bu-t, CH2Ph; R3 = Me, (Me)2CH,; R4 = C6H13, C4F9, C6F13, C8F17, C10F21] (also prepared) and 4-methylphenyl isonitrile and separated by preparative HPLC with a FluofixTM column.

IT **305816-04-0P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(fluorous-tagging strategy for synthesis and separation of mixts. of organic compds.)

RN 305816-04-0 CAPLUS

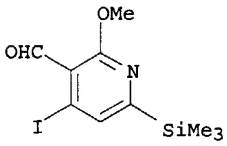
CN Pyridine, 4-iodo-2-methoxy-3-methyl-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(fluorous-tagging strategy for synthesis and separation of mixts. of organic compds.)

RN 174092-75-2 CAPLUS

CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2001:464384 CAPLUS

DN 135:61470

TI Synthesis of camptothecin and related compounds via a novel 4+1 radical annulation

IN Curran, Dennis P.; Bom, David

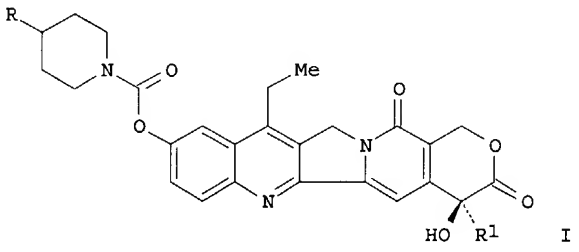
PA University of Pittsburgh, USA

10663605

SO U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 436,799, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6252079	B1	20010626	US 1997-886093	19970702
	US 6211371	B1	20010403	US 1998-7872	19980115
	WO 9901456	A1	19990114	WO 1998-US13941	19980702
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9884761	A1	19990125	AU 1998-84761	19980702
	US 2001029298	A1	20011011	US 2001-815459	20010323
	US 6620937	B2	20030916		
	US 2004063947	A1	20040401	US 2003-663605	20030916
PRAI	US 1993-85190	B2	19930630		
	US 1995-436799	B2	19950508		
	US 1997-886093	A	19970702		
	US 1998-7872	A3	19980115		
	WO 1998-US13941	W	19980702		
	US 2001-815459	A3	20010323		

OS CASREACT 135:61470; MARPAT 135:61470
GI



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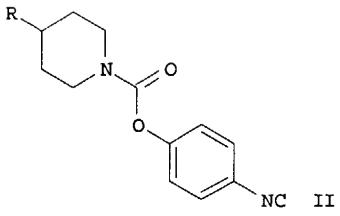

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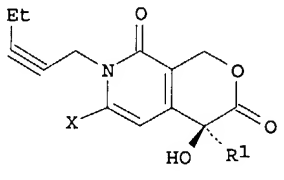


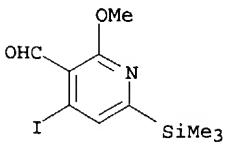
III

AB Camptothecin analogs, such as I [R = H, alkoxy, N containing heterocyclyl, such as piperidinyl; R1 = alkyl, allyl, propargyl, benzyl], were prepared via a novel [4 + 1] radical annulation of the corresponding isonitriles II with pyridinones III [X = Br, iodo] for use as topoisomerase inhibitors. Thus, (+)-irinotecan I [R = piperidinyl, R1 = Et] was prepd in 31% yield by cyclization of isonitrile II [R = piperidinyl] with pyridinone III [R1 = Et, X = I] in the presence of hexadimethylditin in benzene. The prepared compds were tested for topoisomerase I inhibiting activity and cytotoxic activity against HL-60 human promyelocytic leukemic cells and against 833 K human teratocarcinoma cells.

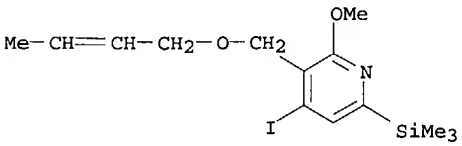
IT **174092-75-2P 174092-76-3P 174092-77-4P**
174092-78-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of camptothecins via radical cyclization for use as topoisomerase inhibitors)

RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA

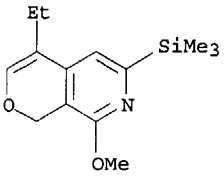
INDEX NAME)



RN 174092-76-3 CAPLUS
CN Pyridine, 3-[(2-butenyloxy)methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

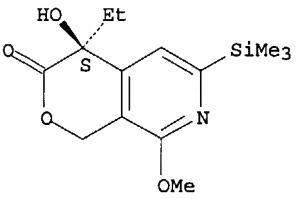


RN 174092-77-4 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 174092-78-5 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

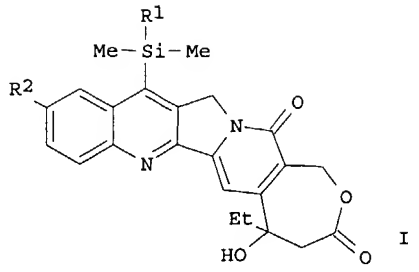


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:70498 CAPLUS
DN 134:266468
TI The combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation
AU Du, Wu; Gabarda, Ana E.; Bom, David; Curran, Dennis P.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Annals of the New York Academy of Sciences (2000), 922(Camptothecins), 317-319
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
OS CASREACT 134:266468

10663605

GI



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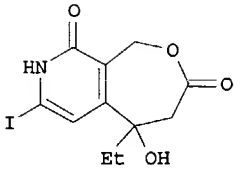

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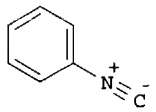


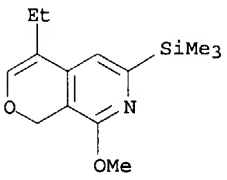
III

AB The authors have developed a practical method for the preparation of diverse homosilatecan analogs, I (R1 = straight hydrocarbon chain, branched hydrocarbon chain, or aryl group and R2 = H, F, MeO, Me, CF3 or AcO). N-Alkylation of iodopyridone II with different propargyl bromides gave compds. that were subjected to a cascade radical annulation with different aryl isonitriles, e.g. III, to give racemic homosilatecans, e.g. I, with two different elements of diversity. More than 100 racemic homosilatecans were prepared by this radical annulation reaction by either the traditional way or a Hewlett-Packard solution phase synthesizer.

IT **174092-77-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation)

RN 174092-77-4 CAPLUS

CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:741925 CAPLUS
DN 133:296587
TI Preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer
IN Curran, Dennis P.; Bom, David; Burke, Thomas G.
PA University of Pittsburgh, USA; University of Kentucky Research Foundation
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061146	A1	20001019	WO 2000-US9401	20000407

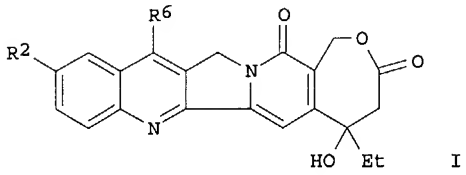
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6207832	B1	20010327	US 1999-290019	19990409
AU 2000042177	A5	20001114	AU 2000-42177	20000407
EP 1173180	A1	20020123	EP 2000-921919	20000407
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002541201	T2	20021203	JP 2000-610479	20000407
NZ 529569	A	20031219	NZ 2000-529569	20000407
NZ 514635	A	20040227	NZ 2000-514635	20000407
US 2001003779	A1	20010614	US 2000-728031	20001130
US 6410731	B2	20020625		
US 2003088101	A1	20030508	US 2002-164326	20020606
PRAI US 1999-290019	A	19990409		
US 1999-290190	A1	19990413		
WO 2000-US9401	W	20000407		
US 2000-728031	A3	20001130		

OS MARPAT 133:296587

GI



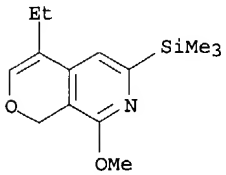
I

AB Camptothecin analogs, such as I [R2 = H, OH, NH2, acyl, alkoxy, acyloxy, etc.; R6 = silyl, silylalkyl, silylalkenyl, silylalkynyl, etc.], were prepared for use as antitumor agents. Thus, (±)-10-amino-7-(tert-butyldimethylsilyl)homocamptothecin, a.k.a. DB 90, was prepared via a multistep synthetic sequence starting from 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, tert-Bu bromoacetate, 1-bromo-3-tert-butyldimethylsilyl-2-propyne, and 4-(tert-Butyloxycabonylamino)phenylisocyanate. The prepared homocamptothecins were tested for activity against MDA-MB-435 tumorigenic metastatic human breast cancer cells.

IT **174092-77-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer)

RN 174092-77-4 CAPLUS

CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

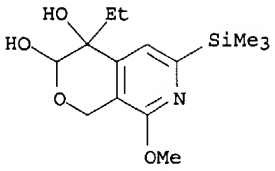


IT **300582-82-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer)

RN 300582-82-5 CAPLUS

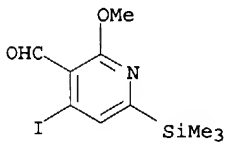
CN 1H-Pyrano[3,4-c]pyridine-3,4-diol, 4-ethyl-3,4-dihydro-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

10663605

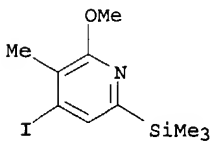


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:632652 CAPLUS
DN 133:350379
TI Solution Phase Synthesis of Libraries of Polycyclic Natural Product Analogues by Cascade Radical Annulation: Synthesis of a 64-Member Library of Mappicine Analogues and a 48-Member Library of Mappicine Ketone Analogues
AU de Frutos, Oscar; Curran, Dennis P.
CS Department of Chemistry and Center for Combinatorial Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Journal of Combinatorial Chemistry (2000), 2(6), 639-649
CODEN: JCCHFF; ISSN: 1520-4766
PB American Chemical Society
DT Journal
LA English
OS CASREACT 133:350379
AB An improved cascade radical annulation route to (±)-mappicine, (S)-mappicine, and mappicine ketone is reported. The route is used to prepare libraries of mappicine and mappicine ketone analogs in a semiautomated fashion. Key diversity generating steps include the addition of an aldehyde to a Grignard reagent derived from a D-ring iodopyridine, N-propargylation of a subsequently derived iodopyridone, and cascade radical annulation with an isonitrile to form a mappicine analog. Parallel oxidation of mappicine analogs produced mappicine ketones. The route is general and flexible and could be used to make very large libraries. It is also illustrative of how late stage cascade reactions can be employed strategically to generate libraries of polycyclic natural product analogs.
IT **174092-75-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(solution phase synthesis of libraries of mappicine and mappicine ketone analogs via cascade radical annulation)
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



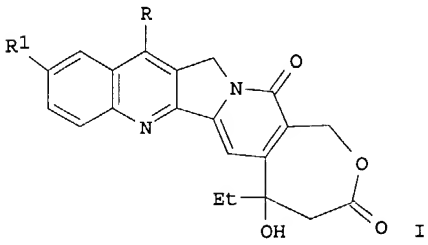
IT **305816-04-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solution phase synthesis of libraries of mappicine and mappicine ketone analogs via cascade radical annulation)
RN 305816-04-0 CAPLUS
CN Pyridine, 4-iodo-2-methoxy-3-methyl-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



10663605

RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:455126 CAPLUS
DN 131:299588
TI Novel A,B,E-Ring-Modified Camptothecins Displaying High Lipophilicity and Markedly Improved Human Blood Stabilities
AU Bom, David; Curran, Dennis P.; Chavan, Ashok J.; Kruszewski, Stefan; Zimmer, Stephen G.; Fraley, Kimberly A.; Burke, Thomas G.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Journal of Medicinal Chemistry (1999), 42(16), 3018-3022
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:299588
GI



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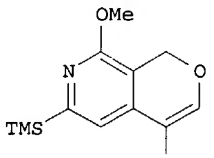
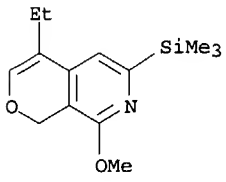


II

AB The camptothecins I (R = Me3CSiMe2, Me3Si; R1 = NH2, OH, H) were prepared starting from enol ether II. A variety of anal. and biophys. methods were employed to compare the blood component interactions and blood stabilities of I with camptothecin. I are potent topoisomerase I inhibitors that are stable not only in the mouse blood but human blood.
IT **174092-77-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel A,B,E-ring-modified camptothecins displaying high lipophilicity and markedly improved human blood stabilities)
RN 174092-77-4 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:48724 CAPLUS
DN 130:125257
TI Synthesis of and intermediates for camptothecins
IN Curran, Dennis P.; Bom, David
PA University of Pittsburgh, USA
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7

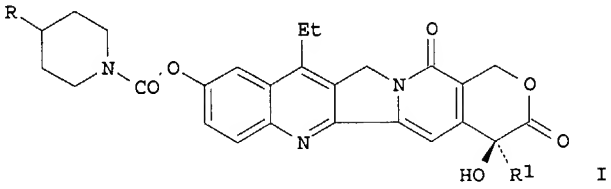
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9901456	A1	19990114	WO 1998-US13941	19980702

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6252079	B1	20010626	US 1997-886093	19970702
AU 9884761	A1	19990125	AU 1998-84761	19980702
PRAI US 1997-886093	A	19970702		
US 1993-85190	B2	19930630		
US 1995-436799	B2	19950508		
WO 1998-US13941	W	19980702		

OS CASREACT 130:125257; MARPAT 130:125257

GI



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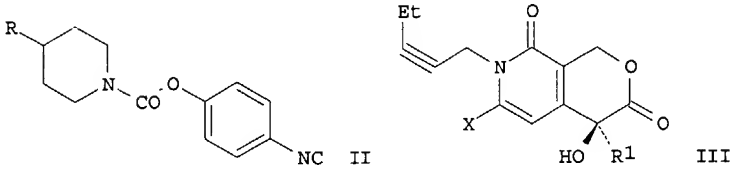
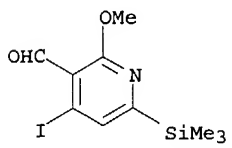


II III

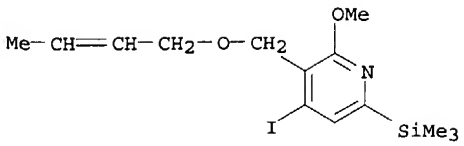
AB Camptothecin analogs, such as I [R = H, alkoxy, N containing heterocyclyl, such as piperidinyl; R1 = allyl, propargyl, benzyl, alkyl], were prepared via a novel [4 + 1] radical annulation of the corresponding isonitriles II with pyridinones III [X = Br, iodo] for use as topoisomerase inhibitors. Thus, (+)-irinotecan I [R = piperidinyl, R1 = Et] was prepd in 31% yield by cyclization of isonitrile II [R = piperidinyl] with pyridinone III [R1 = Et, X = iodo] in the presence of hexadimethylditin in benzene. The prepared compds were tested for topoisomerase I inhibiting activity and cytotoxic activity against HL-60 human promyelocytic leukemic cells and against 833K human teratocarcinoma cells.

IT **174092-75-2P 174092-76-3P 174092-78-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of camptothecins via radical cyclization for use as topoisomerase inhibitors)

RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

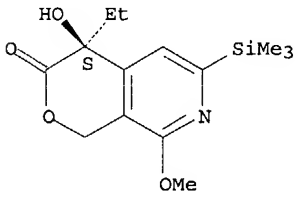


RN 174092-76-3 CAPLUS
CN Pyridine, 3-[(2-butenyloxy)methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



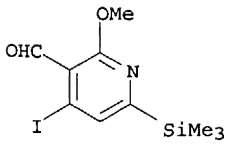
RN 174092-78-5 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

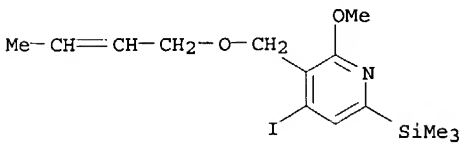


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

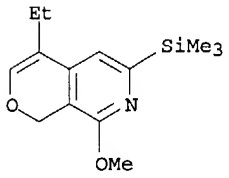
L12 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:63390 CAPLUS
DN 128:154267
TI A general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles
AU Josien, Hubert; Ko, Sung-Bo; Bom, David; Curran, Dennis P.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Chemistry--A European Journal (1998), 4(1), 67-83
CODEN: CEUJED; ISSN: 0947-6539
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
OS CASREACT 128:154267
AB A general and efficient synthesis of (20S)-camptothecin (I) was reported. A key common intermediate containing the pyridone and lactone (DE) rings of camptothecin and most derivs. was constructed from 2-trimethylsilyl-6-methoxypyridine by a series of metalation reactions and a Heck cyclization to provide an achiral bicyclic enol ether. Sharpless asym. dihydroxylation followed by lactol oxidation and iododesilylation produced the key intermediate in 94% enantiomeric excess. Alkylation with propargyl bromide and a cascade radical reaction with PhNC then produced I. About 20 other penta- and hexacyclic analogs of camptothecin with differing single or multiple substituents at C7, C9, C10, C11, and/or C12 were made by changing the propargylating agent and the isonitrile. Included among these are several drug candidates and the approved drugs topotecan and irinotecan. The synthesis of the prodrug irinotecan is a direct one that does not pass through the active metabolite. The use of ortho-trimethylsilyl-substituted isonitriles allows the regioselective synthesis of camptothecin analogs in cases where isomeric mixts. are formed from the parent isonitriles. The synthesis of the derivs. relies on the broad scope and functional group tolerance of the key cascade radical reaction.
IT **174092-75-2P 174092-76-3P 174092-77-4P**
174092-78-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles)
RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 174092-76-3 CAPLUS
CN Pyridine, 3-[(2-butenyloxy)methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

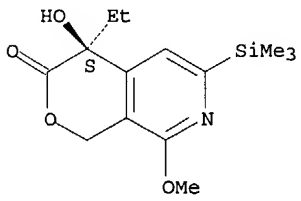


RN 174092-77-4 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



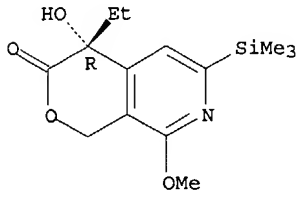
RN 174092-78-5 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **202745-00-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(general synthetic approach to the (20S)-camptothecin family of antitumor agents by a regiocontrolled cascade radical cyclization of aryl isonitriles)
RN 202745-00-4 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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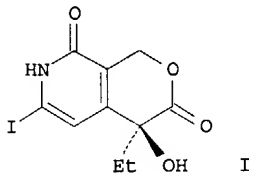
RE.CNT 106 THERE ARE 106 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:48103 CAPLUS
DN 124:176598
TI Cascade radical reactions of isonitriles: a second-generation synthesis of (20S)-camptothecin, topotecan, irinotecan, and GI-147211C
AU Curran, Dennis P.; Ko, Sung-Bo; Josien, Hubert
CS Dep. Chem., Univ. Pittsburgh, Pittsburgh, PA, 15260, USA
SO Angewandte Chemie, International Edition in English (1996), Volume Date 1995, 34(23/24), 2683-4
CODEN: ACIEAY; ISSN: 0570-0833
PB VCH
DT Journal
LA English
OS CASREACT 124:176598
GI

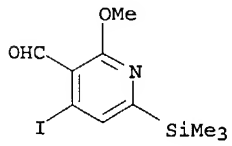


I

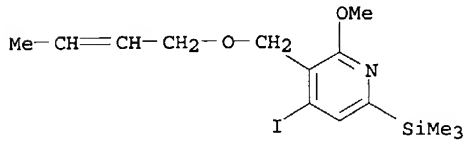
AB A highly convergent second-generation synthesis of the title compds was achieved from 2-bromo-6-methoxypyridine via the lactone I, which was combined with propargyl bromides and aryl isonitriles in as few as two steps.

IT **174092-75-2P 174092-76-3P 174092-77-4P**
174092-78-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cascade radical reactions of isonitriles in the synthesis of camptothecin, topotecan, irinotecan and GI-147211C)

RN 174092-75-2 CAPLUS
CN 3-Pyridinecarboxaldehyde, 4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 174092-76-3 CAPLUS
CN Pyridine, 3-[(2-butenyloxy)methyl]-4-iodo-2-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RN 174092-77-4 CAPLUS
CN 1H-Pyrano[3,4-c]pyridine, 4-ethyl-8-methoxy-6-(trimethylsilyl)- (9CI) (CA INDEX NAME)

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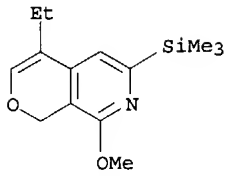

RN 174092-78-5 CAPLUS
CN 3H-Pyrano[3,4-c]pyridin-3-one, 4-ethyl-1,4-dihydro-4-hydroxy-8-methoxy-6-(trimethylsilyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).